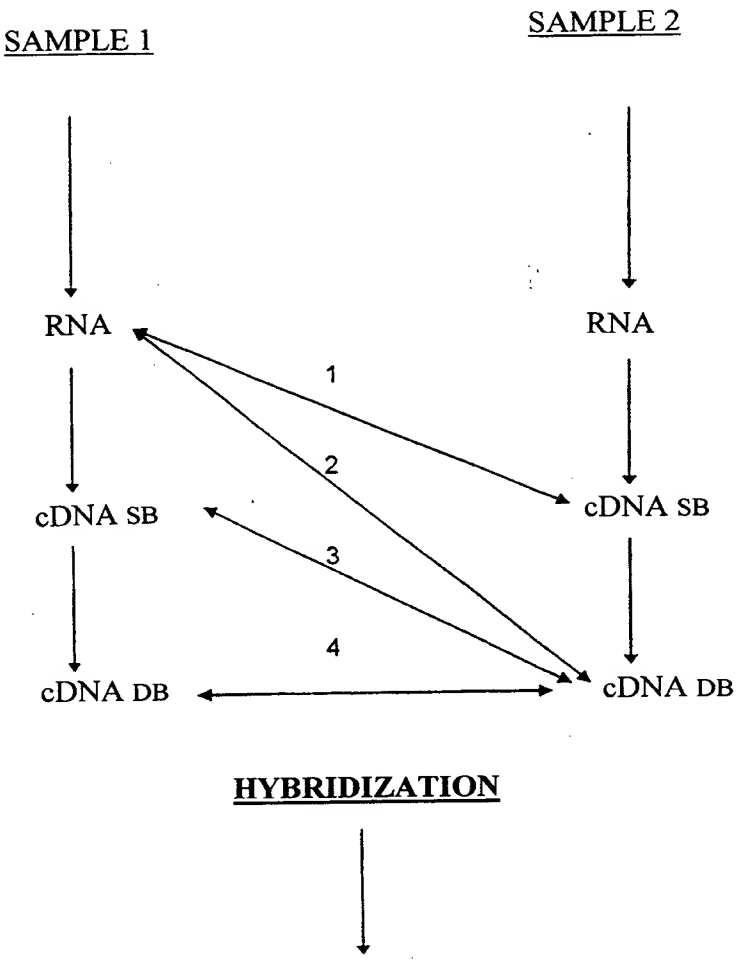

SAMPLE 1
SAMPLE 2
RNA
RNA
1
2
cDNA SB
cDNA SB
3
4
cDNA DB
cDNA DB
HYBRIDIZATION
1. -> HETERODUPLEXES RNA/cDNA SB
2. -> HETEROTRIPLEXES RNA/cDNA DB
3,4. -> HOMODUPLEXES DNA/DNA

FIGURE 1A

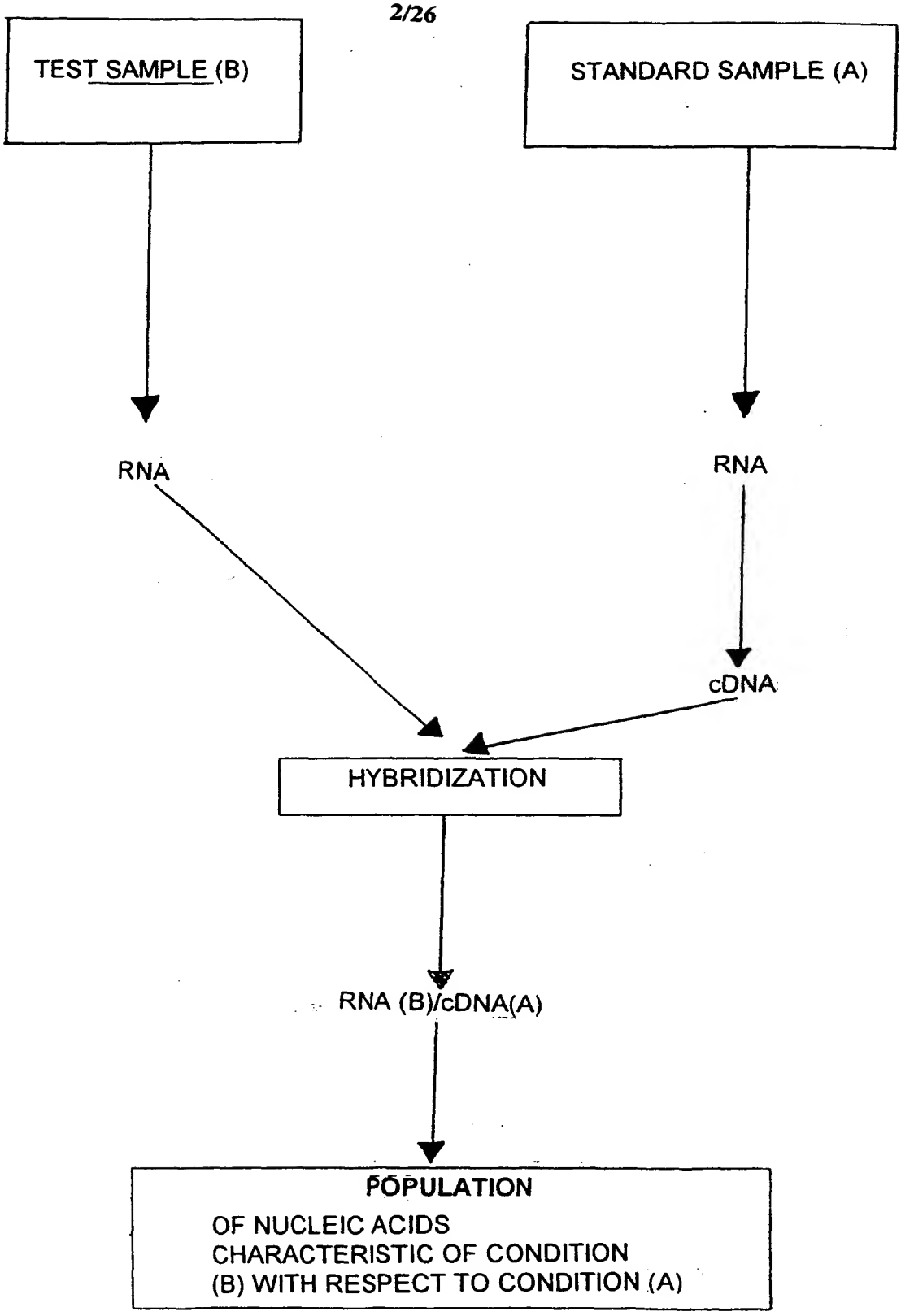
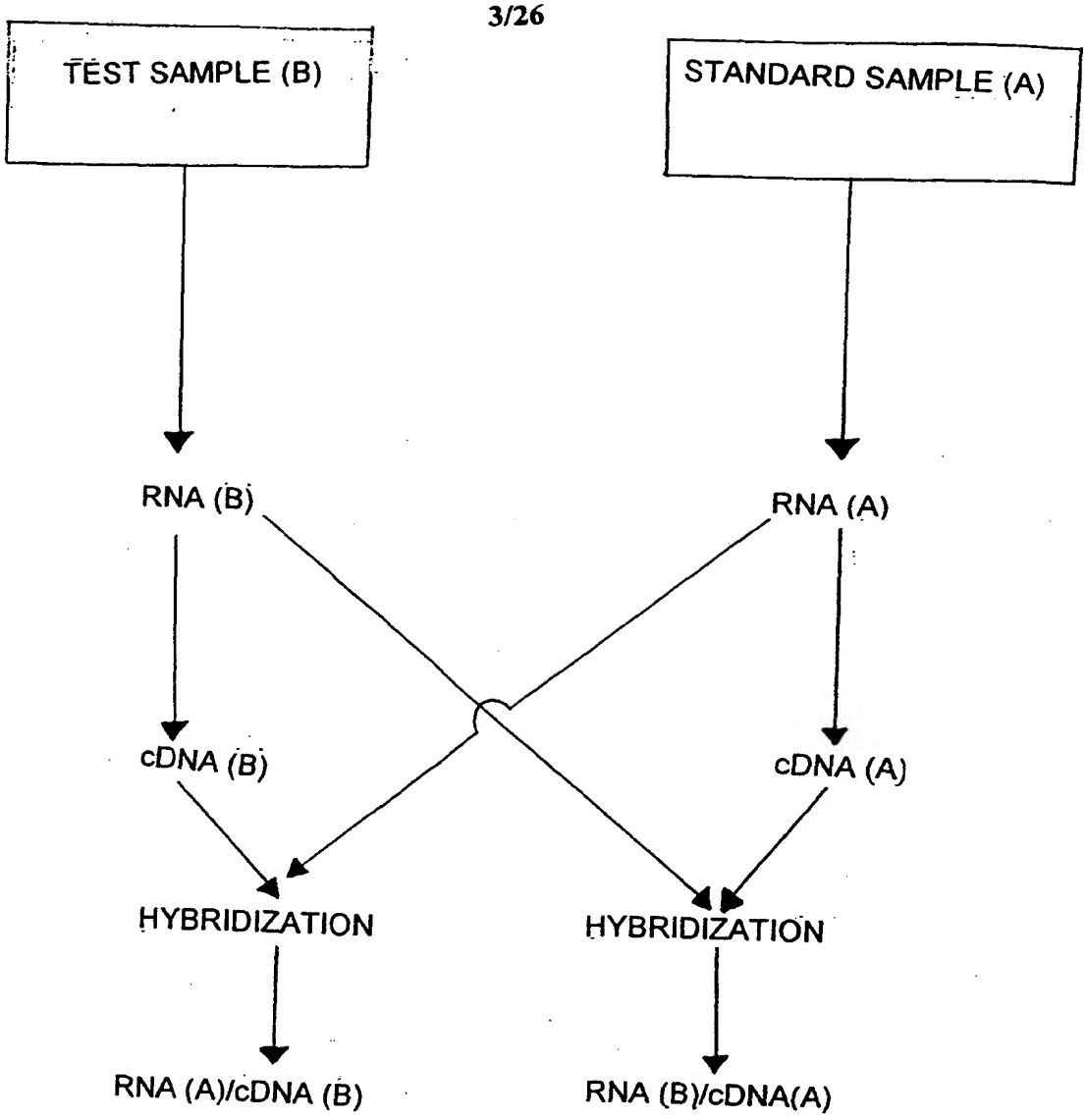

TEST SAMPLE (B)
STANDARD SAMPLE (A)
RNA
RNA
cDNA
HYBRIDIZATION
RNA (B)/cDNA(A)
POPULATION
OF NUCLEIC ACIDS
CHARACTERISTIC OF CONDITION
(B) WITH RESPECT TO CONDITION (A)

FIGURE 1B



POPULATION 2
OF NUCLEIC ACIDS CHARACTERISTIC OF CONDITION (A) SPLICING PATTERNS WITH RESPECT TO CONDITION (B) SPLICING PATTERNS

POPULATION 1
OF NUCLEIC ACIDS CHARACTERISTIC OF CONDITION (B) SPLICING PATTERNS WITH RESPECT TO CONDITION (A) SPLICING PATTERNS

FIGURE 1C

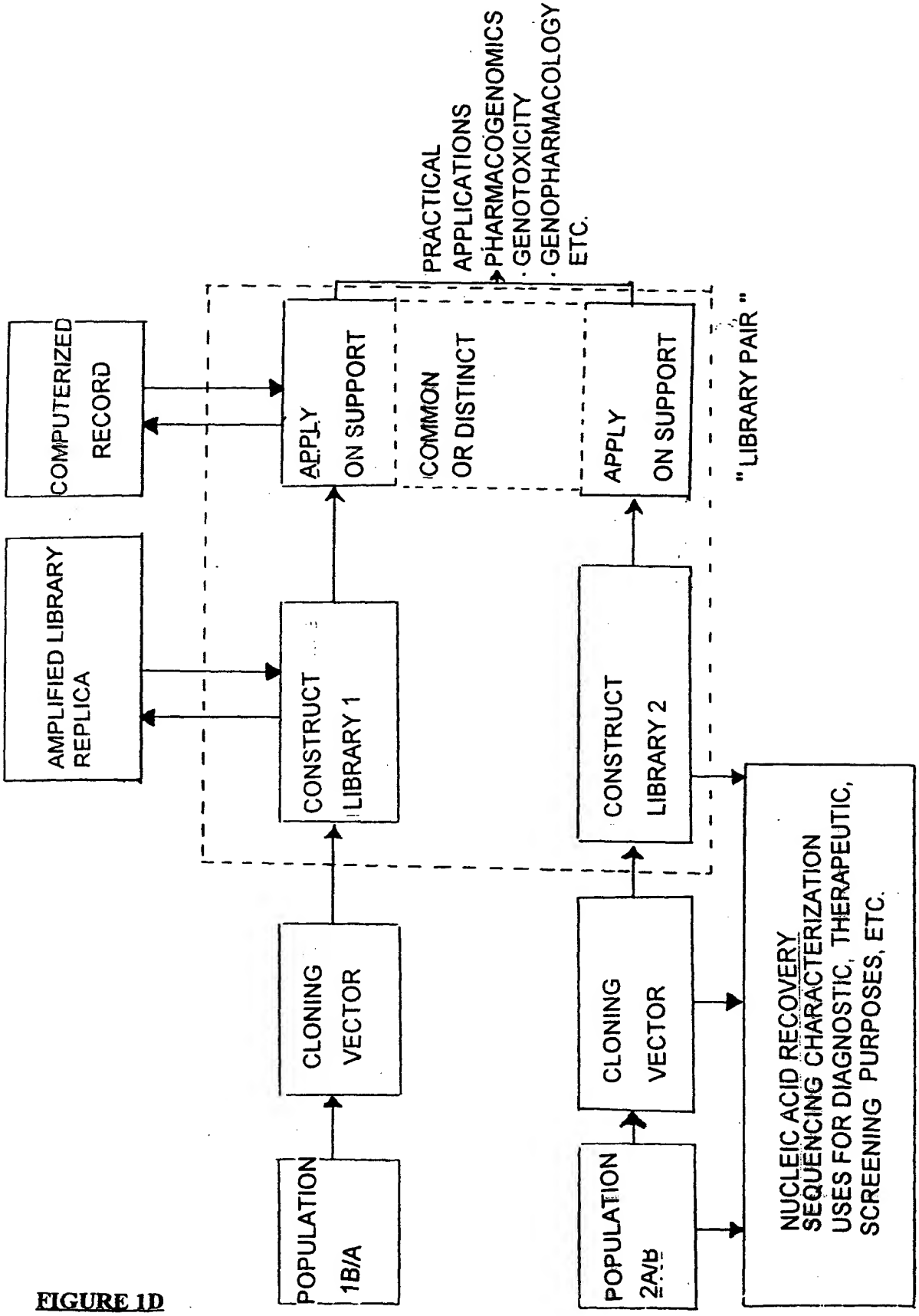

POPULATION 1B/A
CLONING VECTOR
CONSTRUCT LIBRARY 1
AMPLIFIED LIBRARY REPLICA
COMPUTERIZED RECORD
APPLY ON SUPPORT
COMMON OR DISTINCT
POPULATION 2A/B
CLONING VECTOR
CONSTRUCT LIBRARY 2
APPLY ON SUPPORT
"LIBRARY PAIR"
PRACTICAL APPLICATIONS
· PHARMACOGENOMICS
· GENOTOXICITY
· GENOPHARMACOLOGY
ETC.
NUCLEIC ACID RECOVERY
SEQUENCING CHARACTERIZATION
USES FOR DIAGNOSTIC, THERAPEUTIC, SCREENING PURPOSES, ETC.

FIGURE 1D

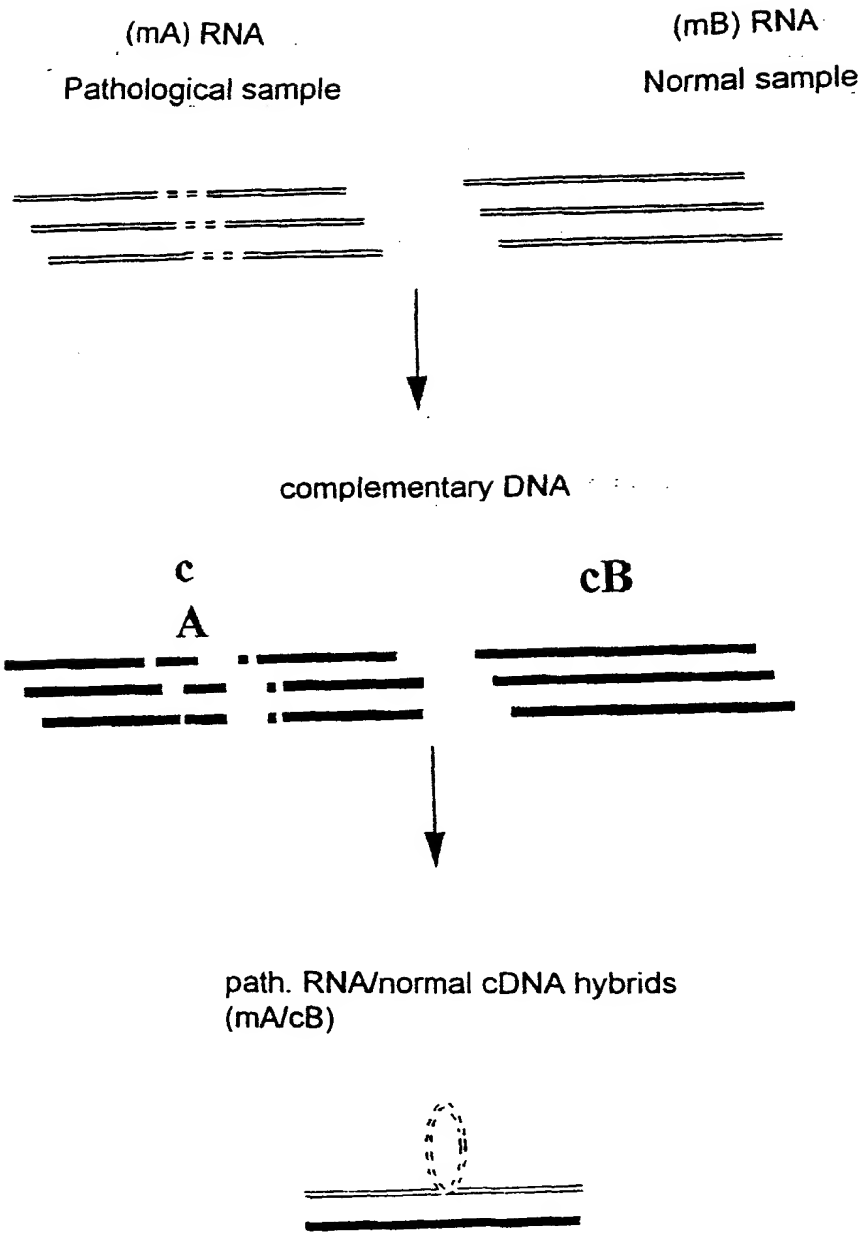
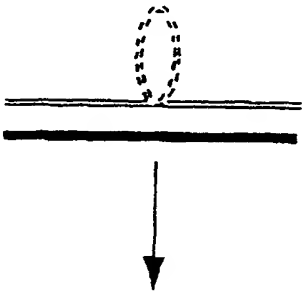

(mA) RNA
Pathological sample
(mB) RNA
Normal sample
complementary DNA
c
A
cB
path. RNA/normal cDNA hybrids
(mA/cB)

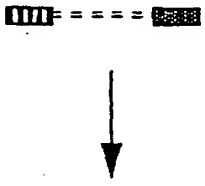
FIGURE 2

path. RNA/normal cDNA hybrids

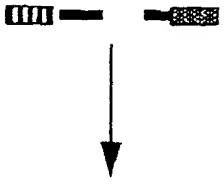


non spliced sequences after RNase H digestion

desired sequence which is 5'- and 3'-labelled by two oligonucléotides



PCR-amplified fragment



cloning and sequencing

FIGURE 3

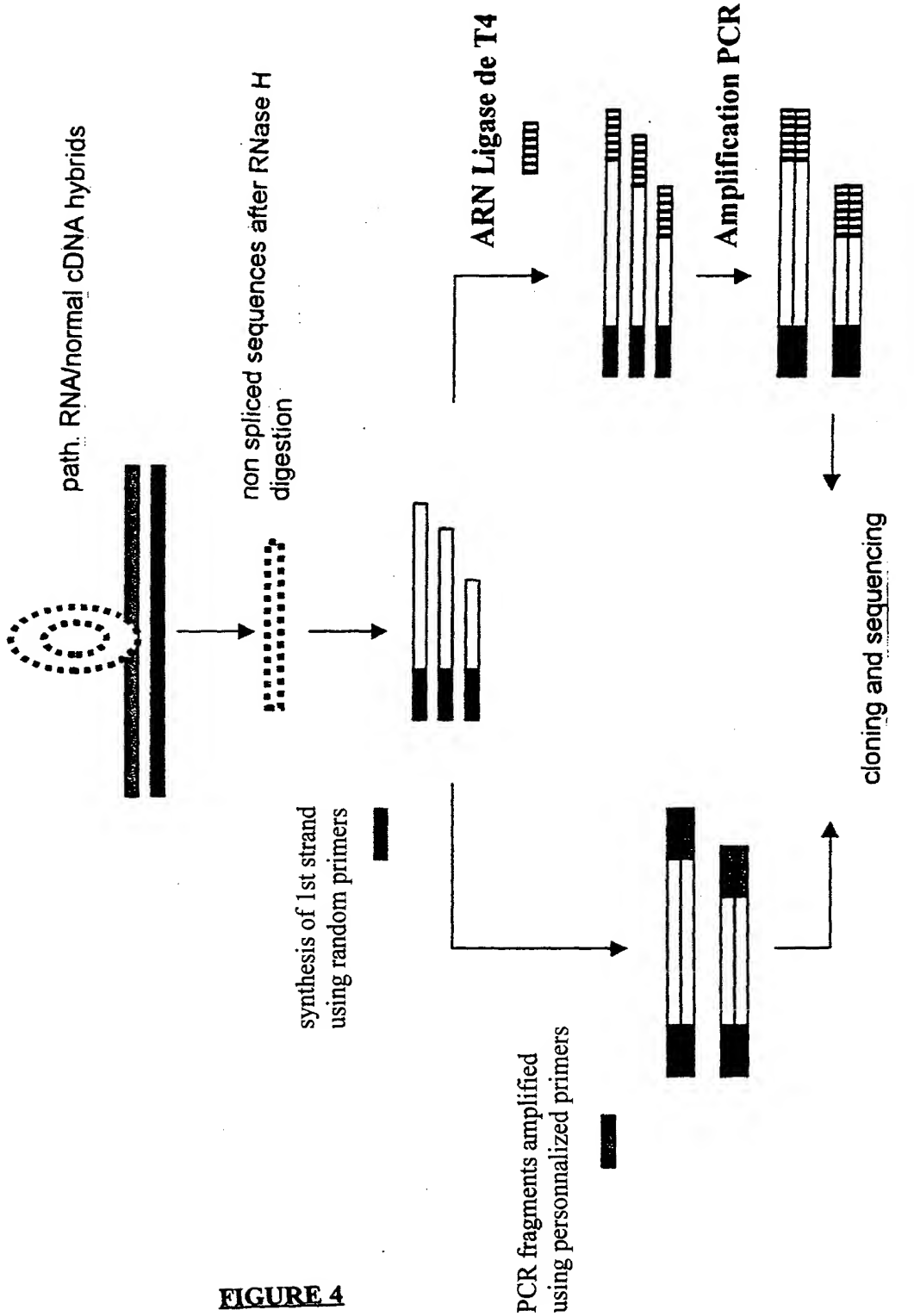

path. RNA/normal cDNA hybrids
non spliced sequences after RNase H digestion
ARN Ligase de T4
Amplification PCR
cloning and sequencing
synthesis of 1st strand using random primers
PCR fragments amplified using personnalized primers

FIGURE 4

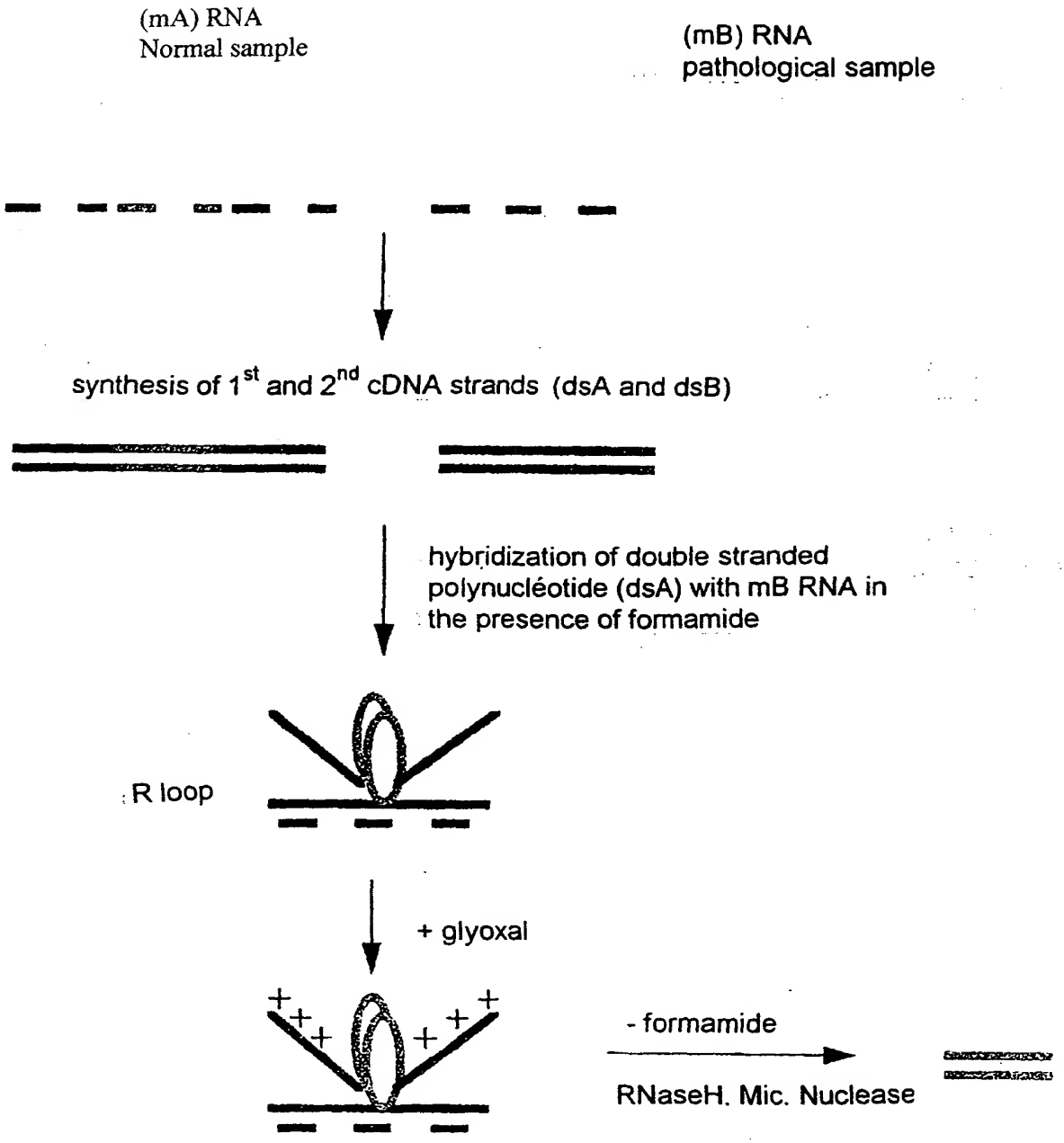

(mA) RNA
Normal sample
(mB) RNA
pathological sample
synthesis of 1st and 2nd cDNA strands (dsA and dsB)
hybridization of double stranded polynucléotide (dsA) with mB RNA in the presence of formamide
R loop
+ glyoxal
- formamide
RNaseH. Mic. Nuclease

FIGURE 5

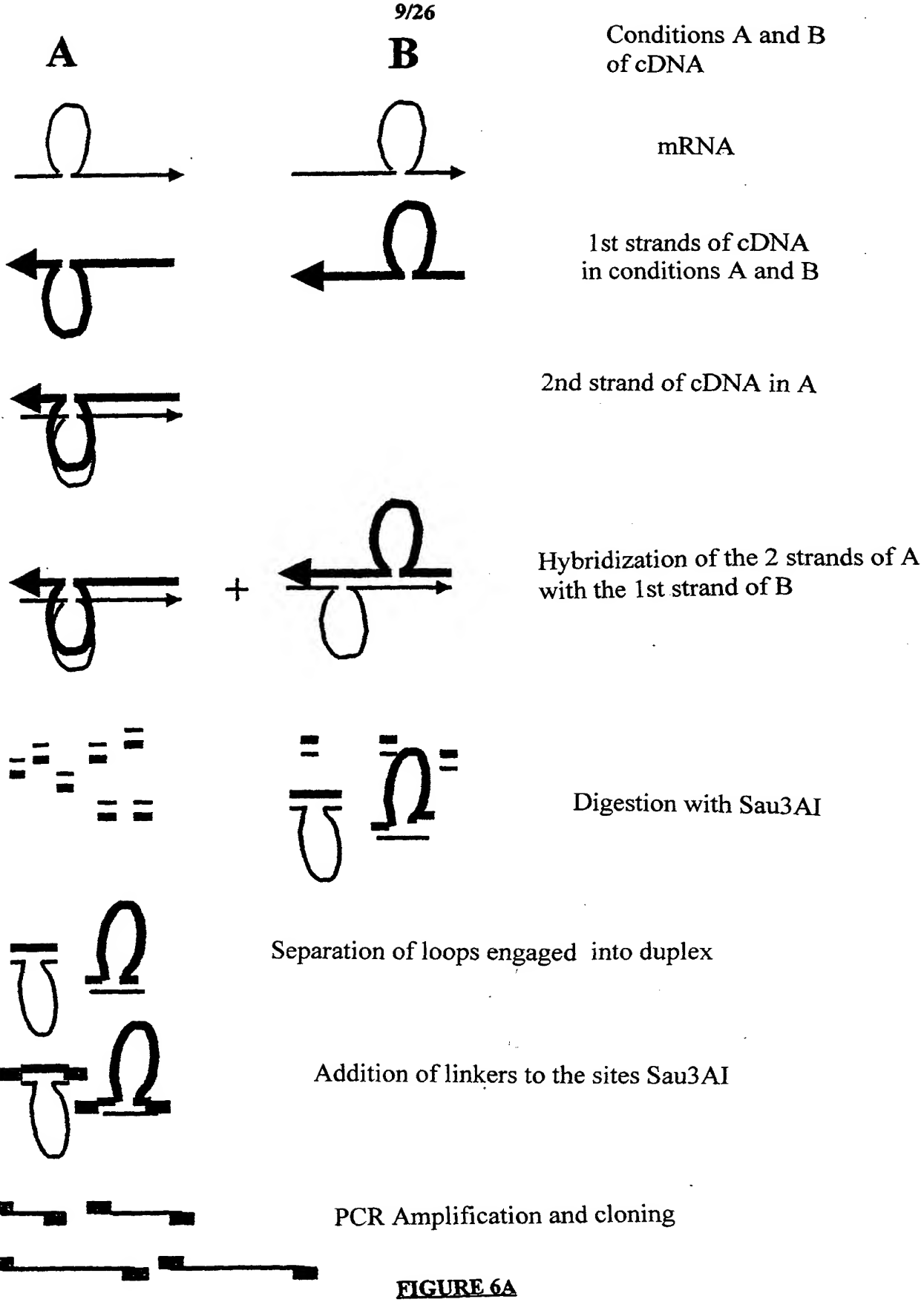

A
B
Conditions A and B of cDNA
mRNA
1st strands of cDNA in conditions A and B
2nd strand of cDNA in A
Hybridization of the 2 strands of A with the 1st strand of B
Digestion with Sau3AI
Separation of loops engaged into duplex
Addition of linkers to the sites Sau3AI
PCR Amplification and cloning

FIGURE 6A

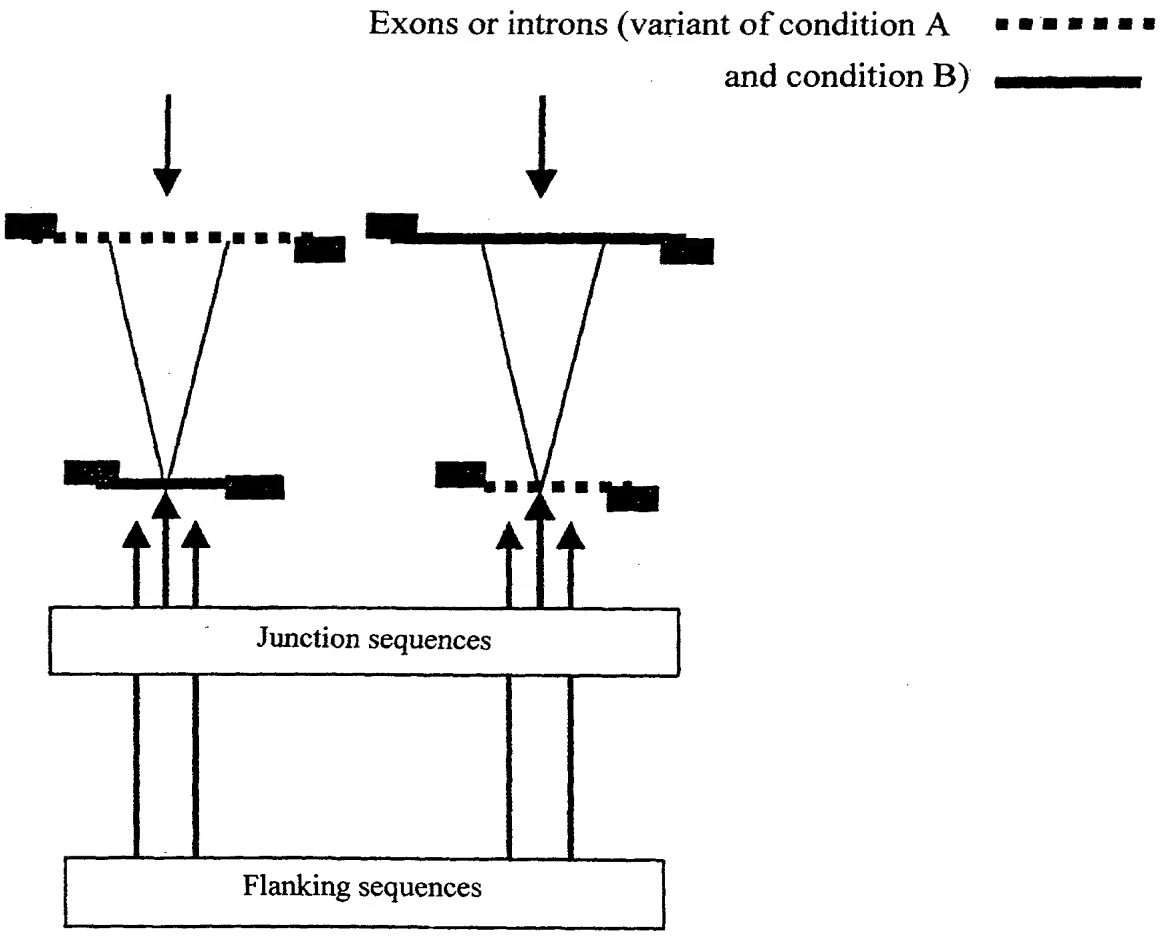

Exons or introns (variant of condition A and condition B)
Junction sequences
Flanking sequences

FIGURE 6B

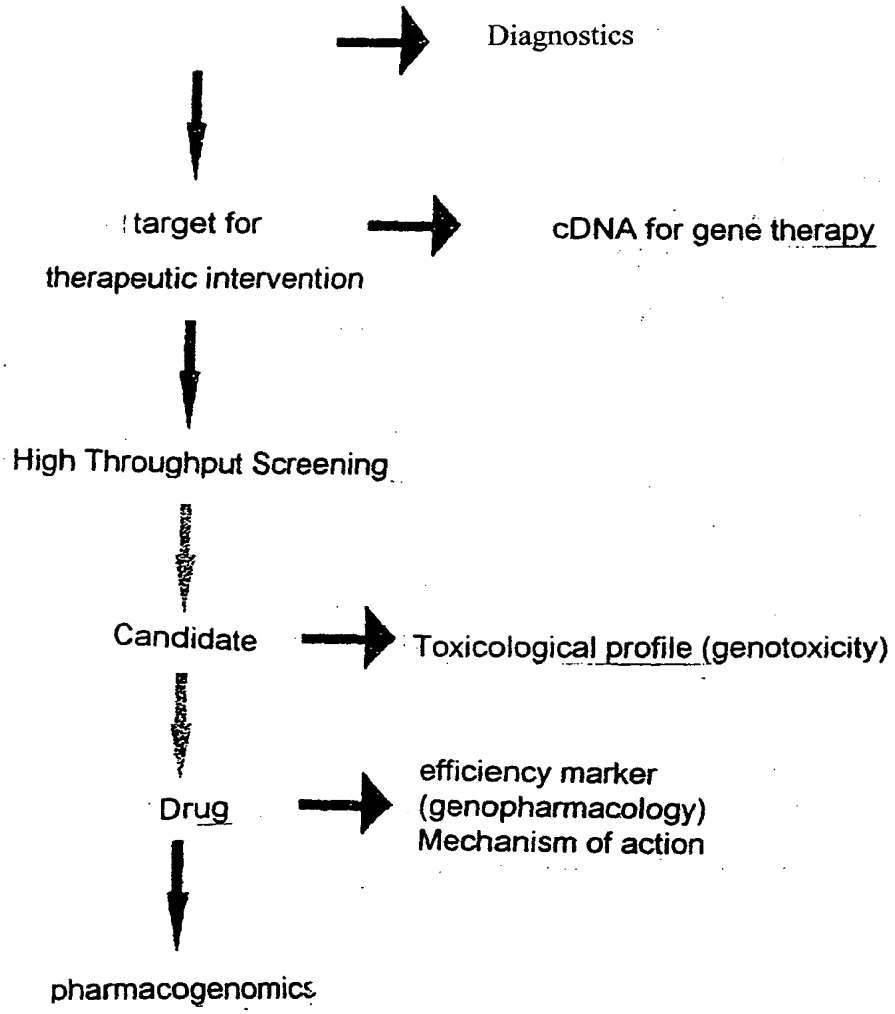
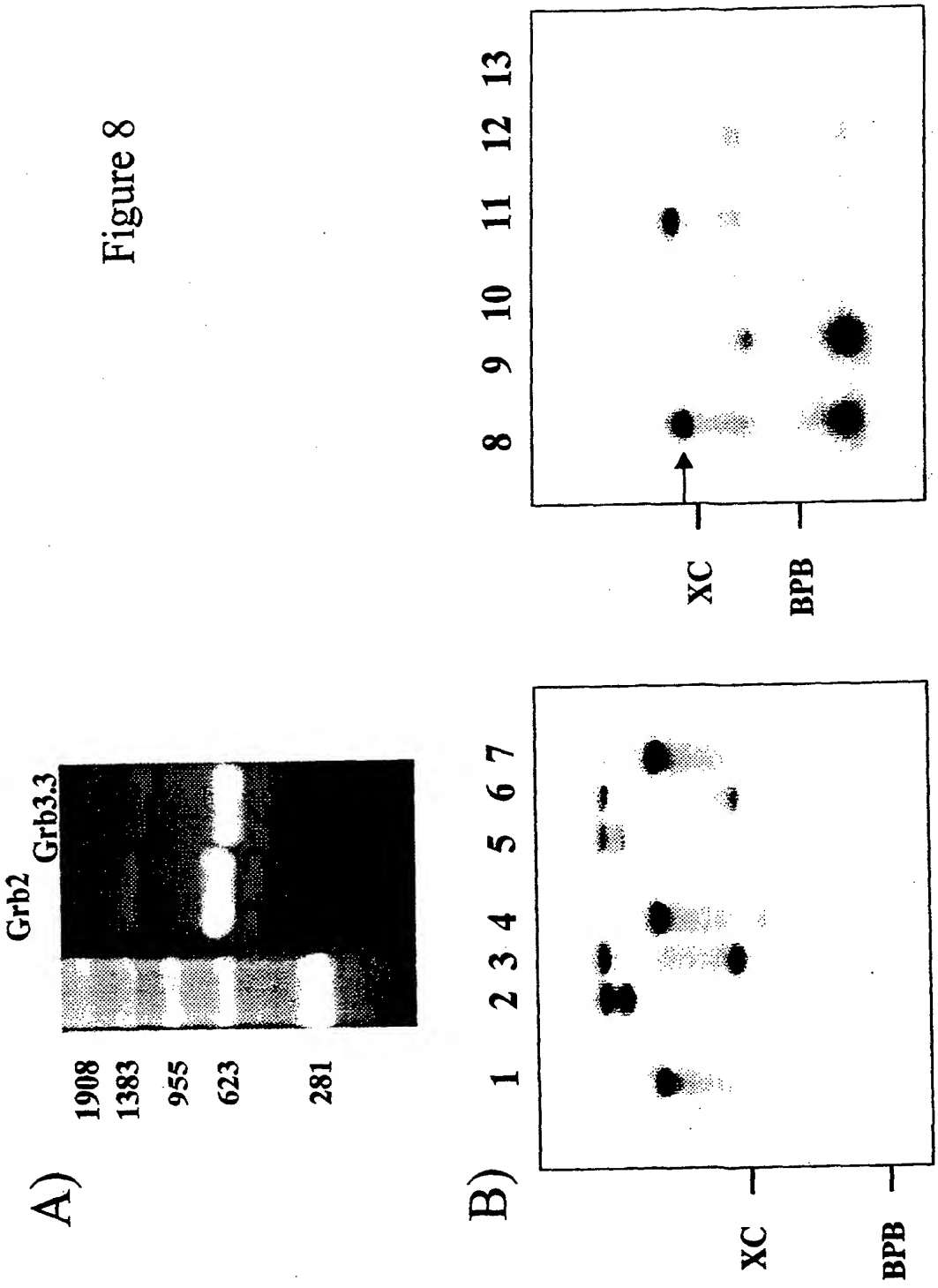
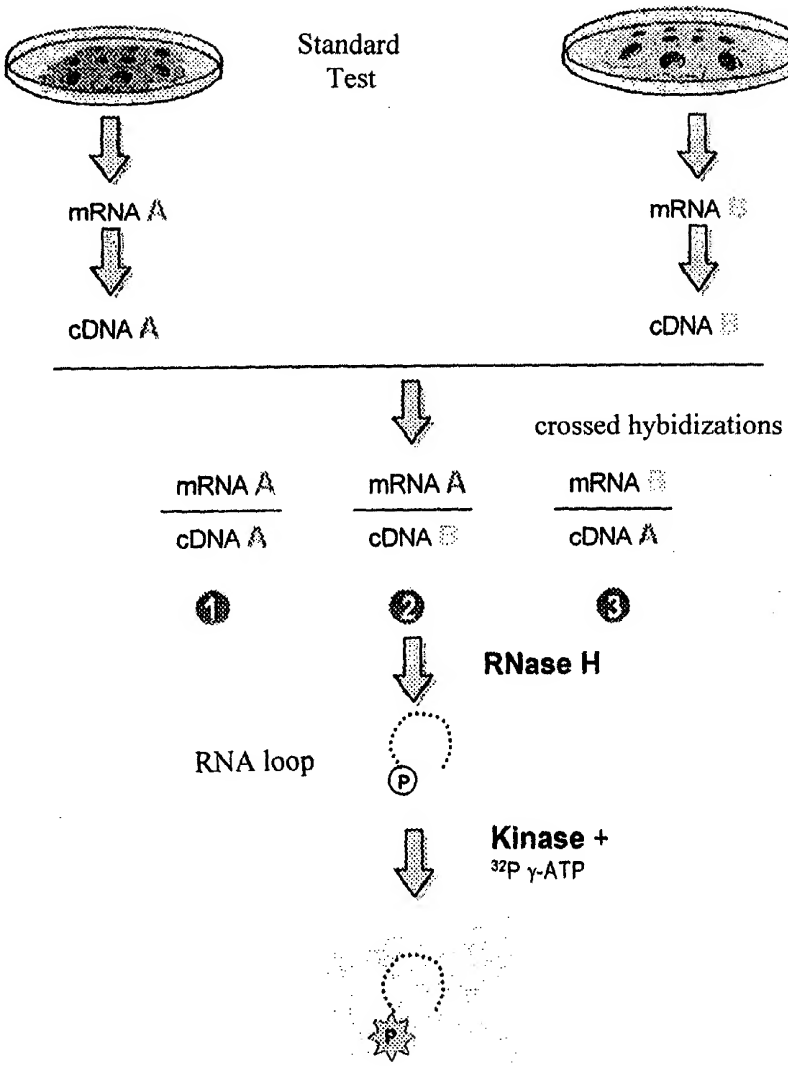

Diagnostics
target for
therapeutic intervention
cDNA for gene therapy
High Throughput Screening
Candidate
Toxicological profile (genotoxicity)
Drug
efficiency marker
(genopharmacology)
Mechanism of action
pharmacogenomics

FIGURE 7

Figure 8


A)
Grb2
Grb3.3
1908
1383
955
623
281
B)
1 2 3 4 5 6 7
XC
BPB
8 9 10 11 12 13
XC
BPB


Standard
Test
Sample
Test
mRNA A
mRNA B
cDNA A
cDNA B
crossed hybidizations
mRNA A
cDNA A
mRNA A
cDNA B
mRNA B
cDNA A
1
2
3
RNase H
RNA loop
P
Kinase +
32P γ-ATP
P

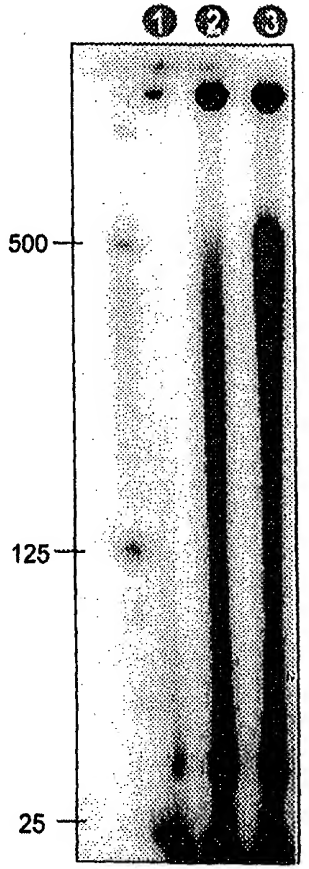

1
2
3
500
125
25

Figure 9

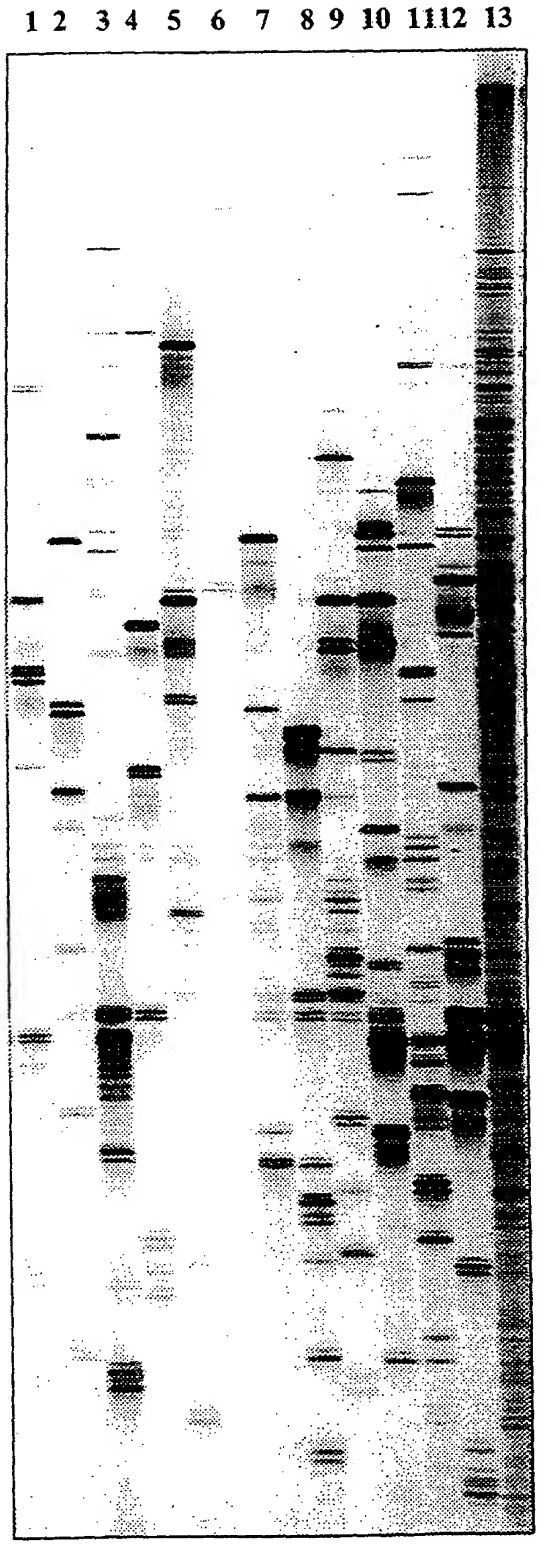
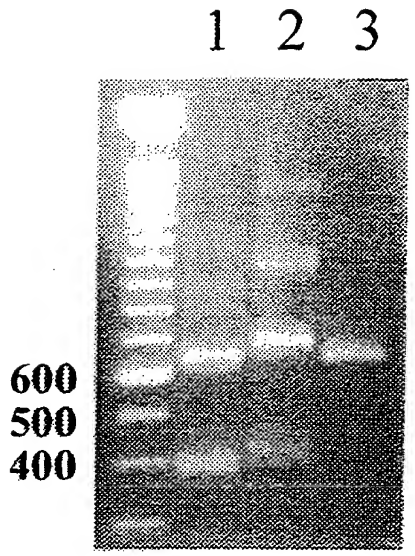


Figure 10

A)



B)

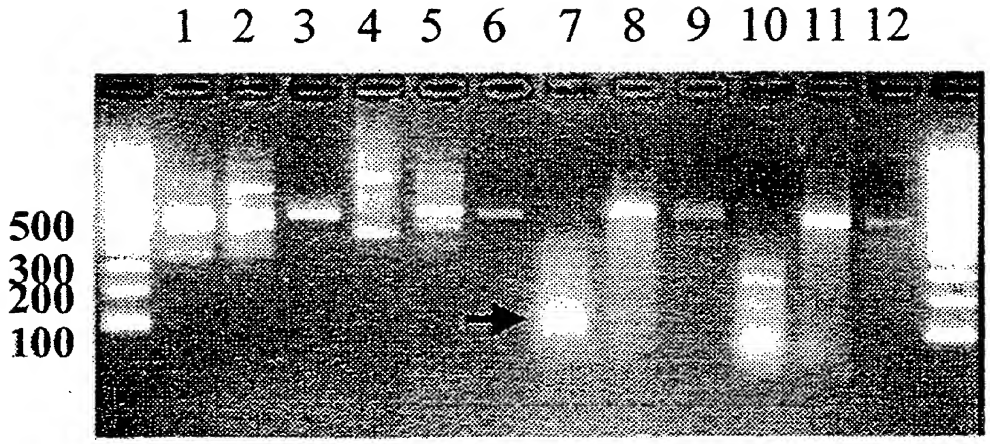


Figure 11

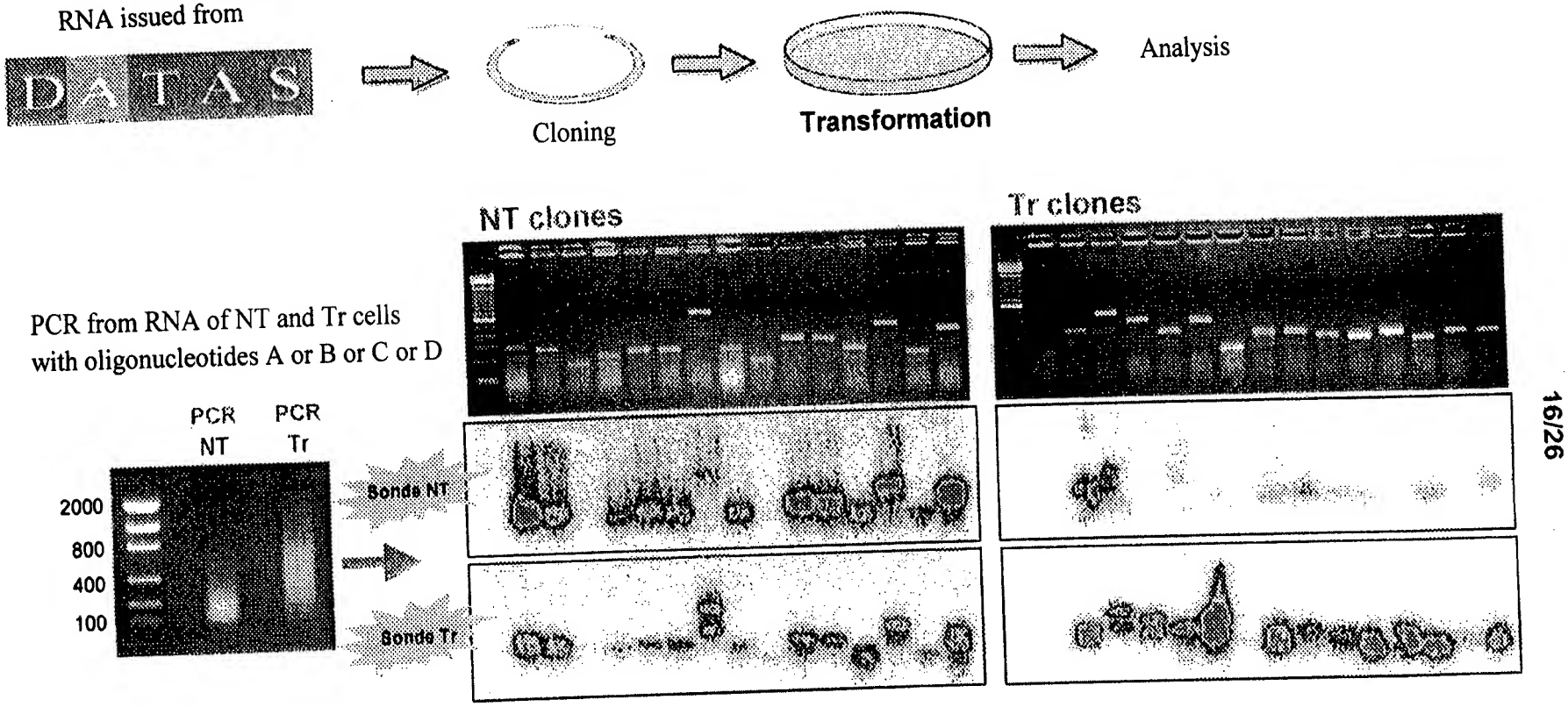

RNA issued from
DATAS
Cloning
Transformation
Analysis
NT clones
Tr clones
PCR from RNA of NT and Tr cells
with oligonucleotides A or B or C or D
PCR NT
PCR Tr
2000
800
400
100
Sonde NT
Sonde Tr

Figure 12

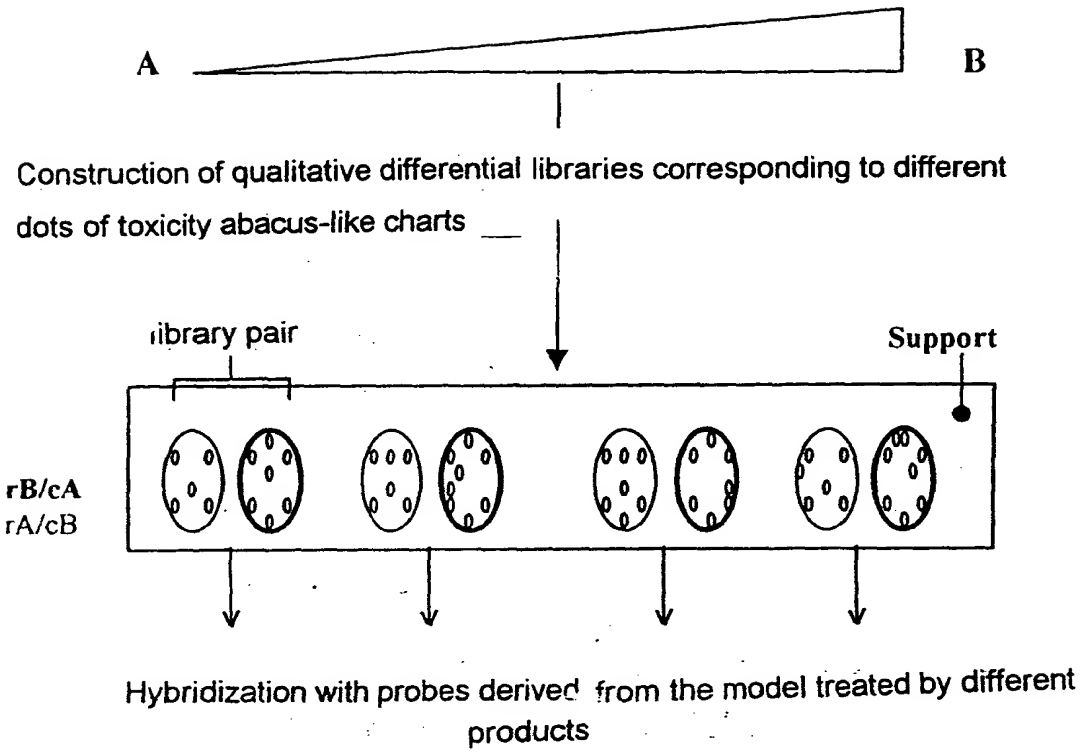

A
B
Construction of qualitative differential libraries corresponding to different dots of toxicity abacus-like charts
library pair
Support
rB/cA
rA/cB
Hybridization with probes derived from the model treated by different products
Product X
Product Y
Product Z

FIGURE 13

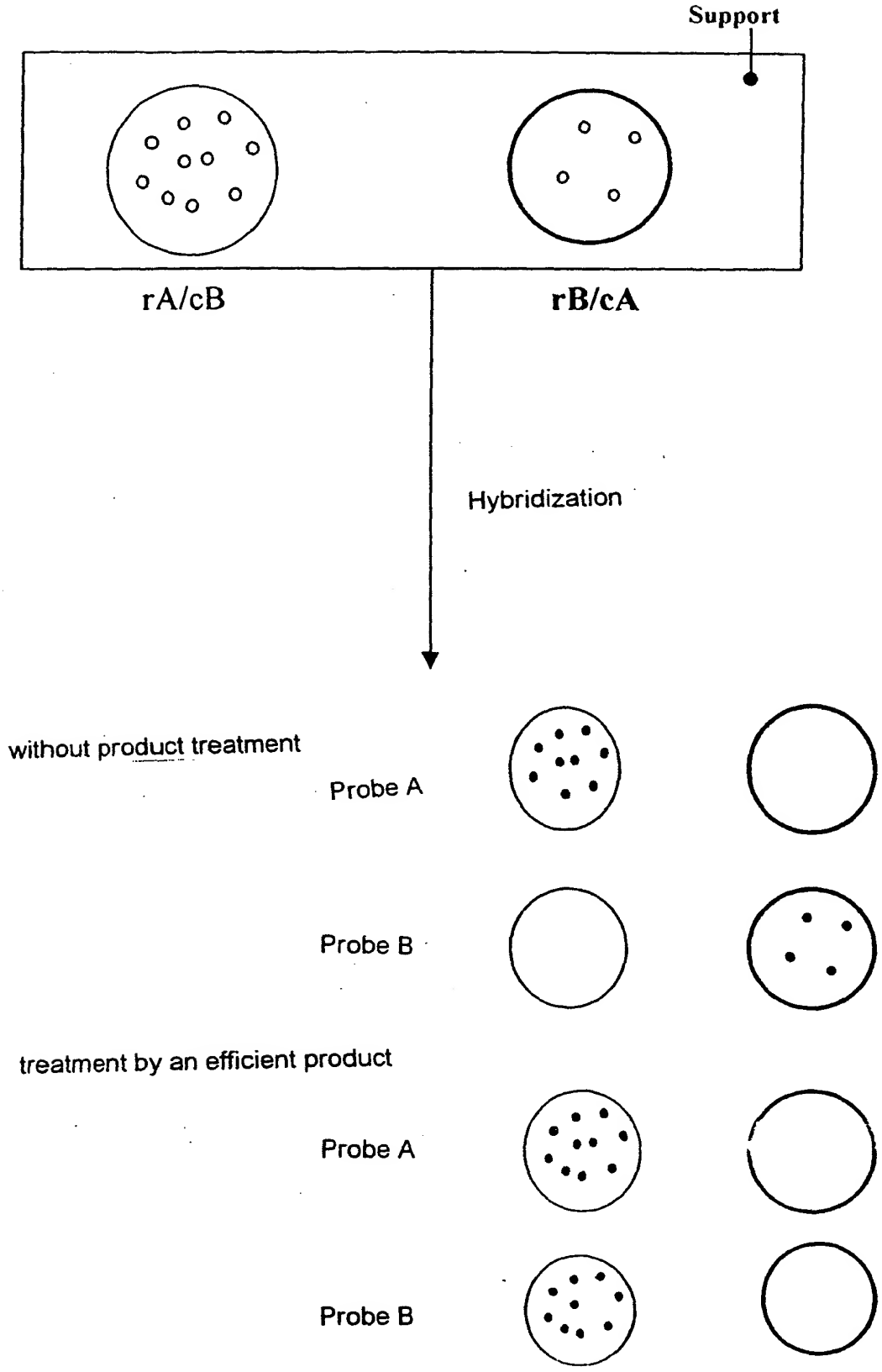

Support
rA/cB
rB/cA
Hybridization
without product treatment
Probe A
Probe B
treatment by an efficient product
Probe A
Probe B

FIGURE 14

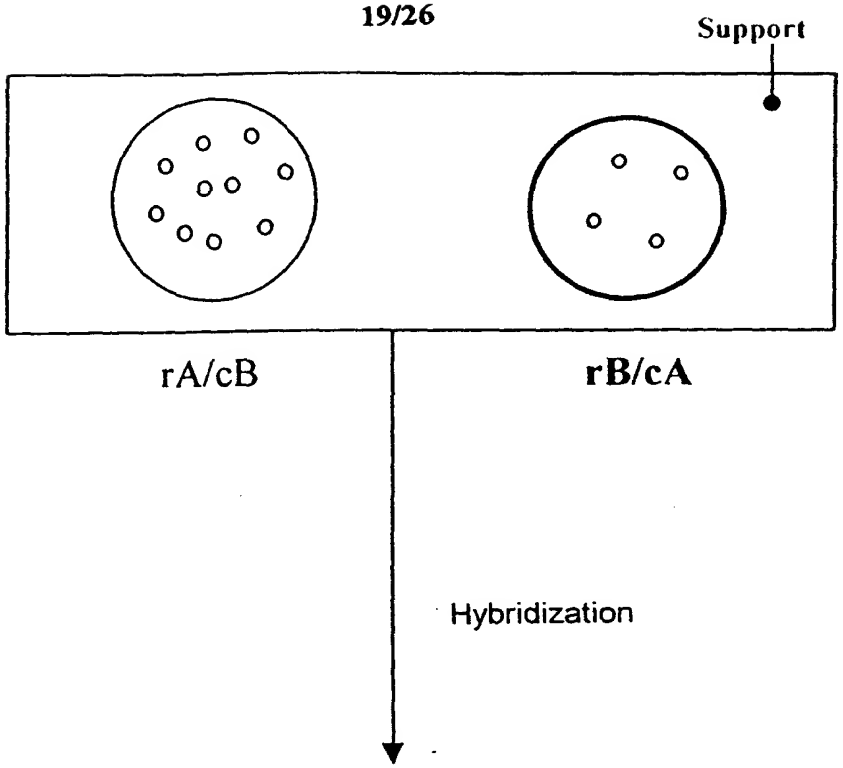

Support
rA/cB
rB/cA
Hybridization
responder-derived biopsy samples
unresponder-derived biopsy samples

FIGURE 15

09/623828

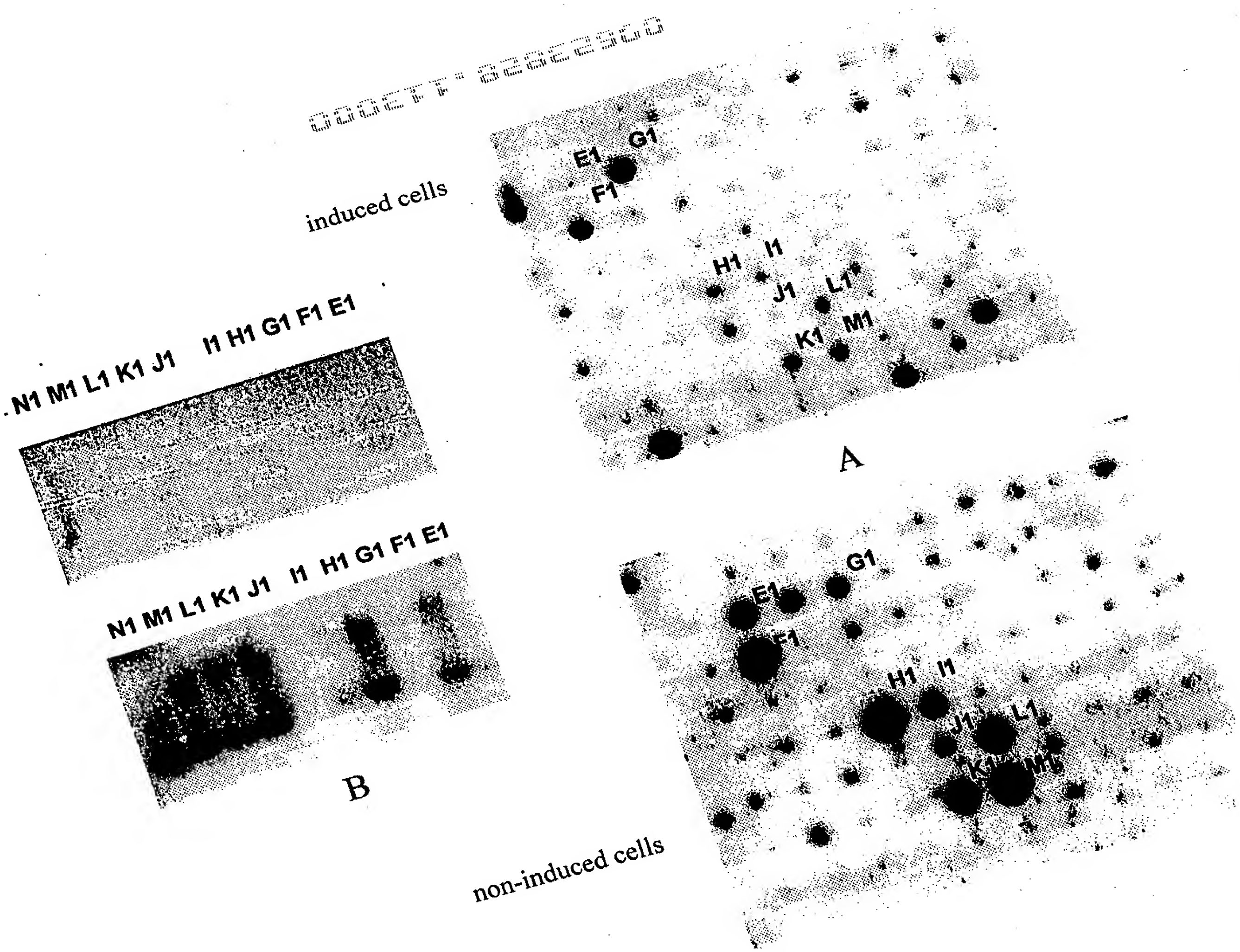


Figure 16

Peptidic Sequence of ΔSHC (SEQ ID NO: 9)

1

MNKLSGGGGR RTRVEGGQLG GEEWTRHGSF VNKPTRGWLH PNDKVMGPGV
SYLVRYMGCV EVLQSMRALD FNTRTQVTRE AISLVCEAVP GAKGATRRRK
PCSRPLSSIL GRSNLKFAGM PITLTVSTSS LNLMAADCKQ IIANHHMQSI
SFASGGDPDT AEYVAYVAKD PVNQRACHIL ECPEGLAQDV ISTIGQAFEL
RFKQYLRNPP KLVTPHDRMA GFDGSAWDEE EEEPPDHQYY NDFPGKEPPL
GGVVDMRLRE GAAPGAARPT APNAQTPSHL GATLPVGQPV GGDPEVRKQM
PPPPPCPGRE LFDDPSYVNV QNLDKARQAV GGAGPPNPAI NGSAPRDLFD
MKPFEDALRV PPPPQSVSMA EQLRGEPWFH GKLSRREAEA LLQLNGDFLV
RTKDHRFESV SHLISYHMDN HLPIISAGSE LCLQQPVERKL

441

Nucleic Sequence of ΔSHC (SEQ ID NO: 10)

atgaacaagc tgagtggagg cggcgggcgc aggactcggg tggaaggggg 50
ccagcttggg ggcgaggagt ggacccgcca cgggagcttt gtcaataagc 100
ccacgcgggg ctggctgcat cccaacgaca aagtcatggg acccggggtt 150
tcctacttgg ttcggtacat gggttgtgtg gaggtcctcc agtcaatgcg 200
tgccctggac ttcaacaccc ggactcaggt caccagggag gccatcagtc 250
tggtgtgtga ggctgtgccg ggtgctaagg gggcgacaag gaggagaaag 300
ccctgtagcc gcccgctcag ctctatcctg gggaggagta acctgaaatt 350
tgctggaatg ccaatcactc tcaccgtctc caccagcagc ctcaacctca 400
tggccgcaga ctgcaaacag atcatcgcca accaccacat gcaatctatc 450
tcatttgcat ccggcgggga tccggacaca gccgagtatg tcgcctatgt 500
tgccaaagac cctgtgaatc agagagcctg ccacattctg gagtgtcccg 550
aagggcttgc ccaggatgtc atcagcacca ttggccaggc cttcgagttg 600
cgcttcaaac aatacctcag gaacccaccc aaactggtca cccctcatga 650
caggatggct ggctttgatg gctcagcatg ggatgaggag gaggaagagc 700
cacctgacca tcagtactat aatgacttcc cggggaagga acccccccttg 750
ggggggggtgg tagacatgag gcttcgggaa ggagccgctc caggggctgc 800
tcgacccact gcacccaatg cccagacccc cagccacttg ggagctacat 850
tgcctgtagg acagcctgtt gggggagatc cagaagtccg caaacagatg 900

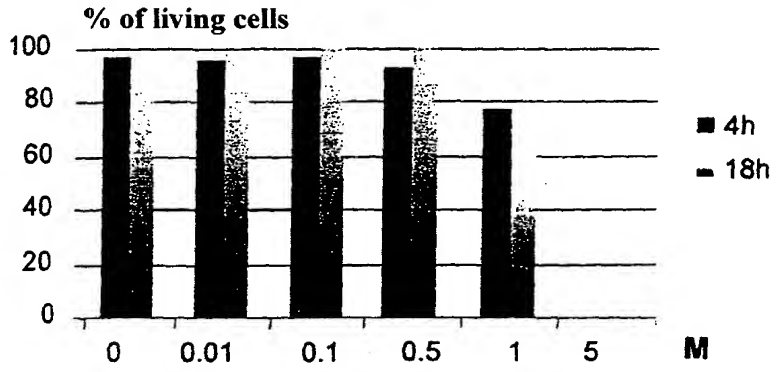
FIGURE 17A

```
ccacctccac caccctgtcc aggcagagag ctttttgatg atccctccta  950
tgtcaacgtc cagaacctag acaaggcccg gcaagcagtg ggtggtgctg 1000
ggcccccaa tcctgctatc aatggcagtg caccccggga cctgtttgac 1050
atgaagccct tcgaagatgc tcttcgggtg cctccacctc cccagtcggt 1100
gtccatggct gagcagctcc gaggggagcc ctggttccat gggaagctga 1150
gccggcggga ggctgaggca ctgctgcagc tcaatgggga cttcttggtt 1200
cggactaagg atcaccgctt tgaaagtgtc agtcacctta tcagctacca 1250
catggacaat cacttgccca tcatctctgc gggcagcgaa ctgtgtctac 1300
agcaacctgt ggagcggaaa ctgtga                           1326
```

FIGURE 17B

HepG2 / Ethanol

Trypan Blue



MTT Test

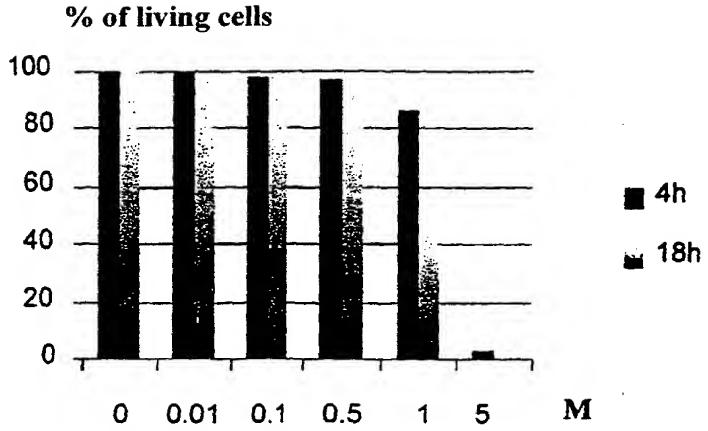
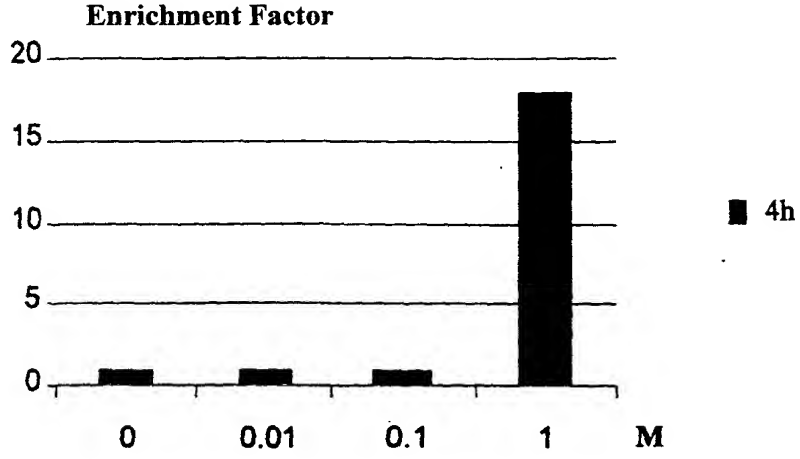


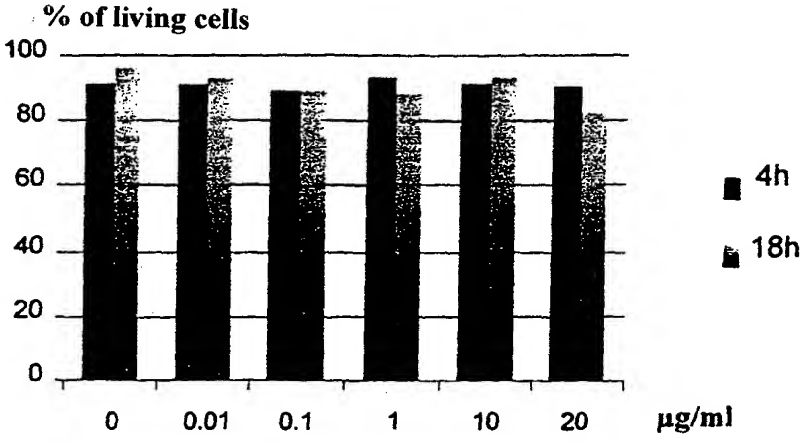
FIGURE 18A

ELISA Test - Fragmentation of DNA



HepG2 / Camptothecin

Trypan Blue



MTT Test

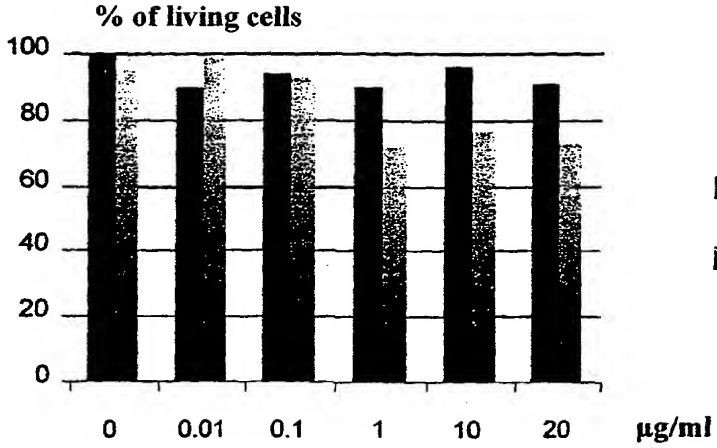
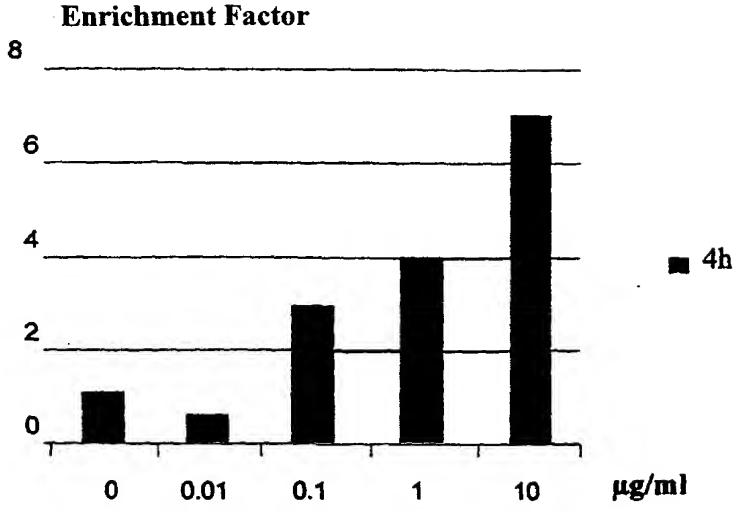


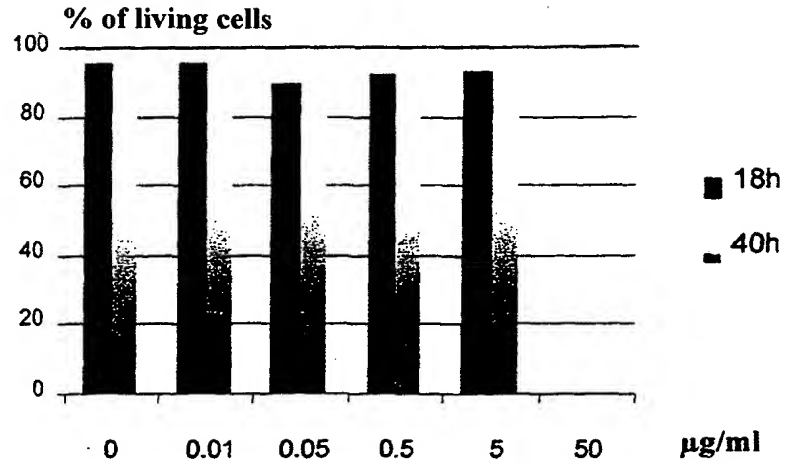
FIGURE 18B

ELISA Test - Fragmentation of DNA

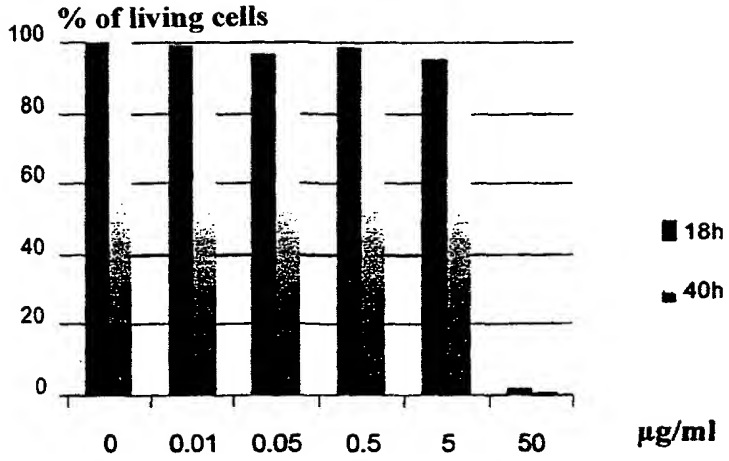


HepG2 / PMA

Trypan Blue



Test MTT



ELISA Test - Fragmentation of DNA

FIGURE 18C

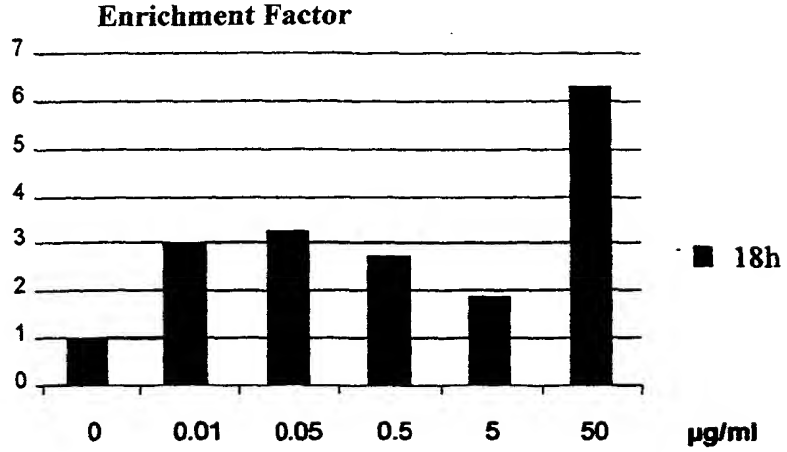


Figure 19